

To Stress or Not.....

Considerations for perioperative steroid stress dosing

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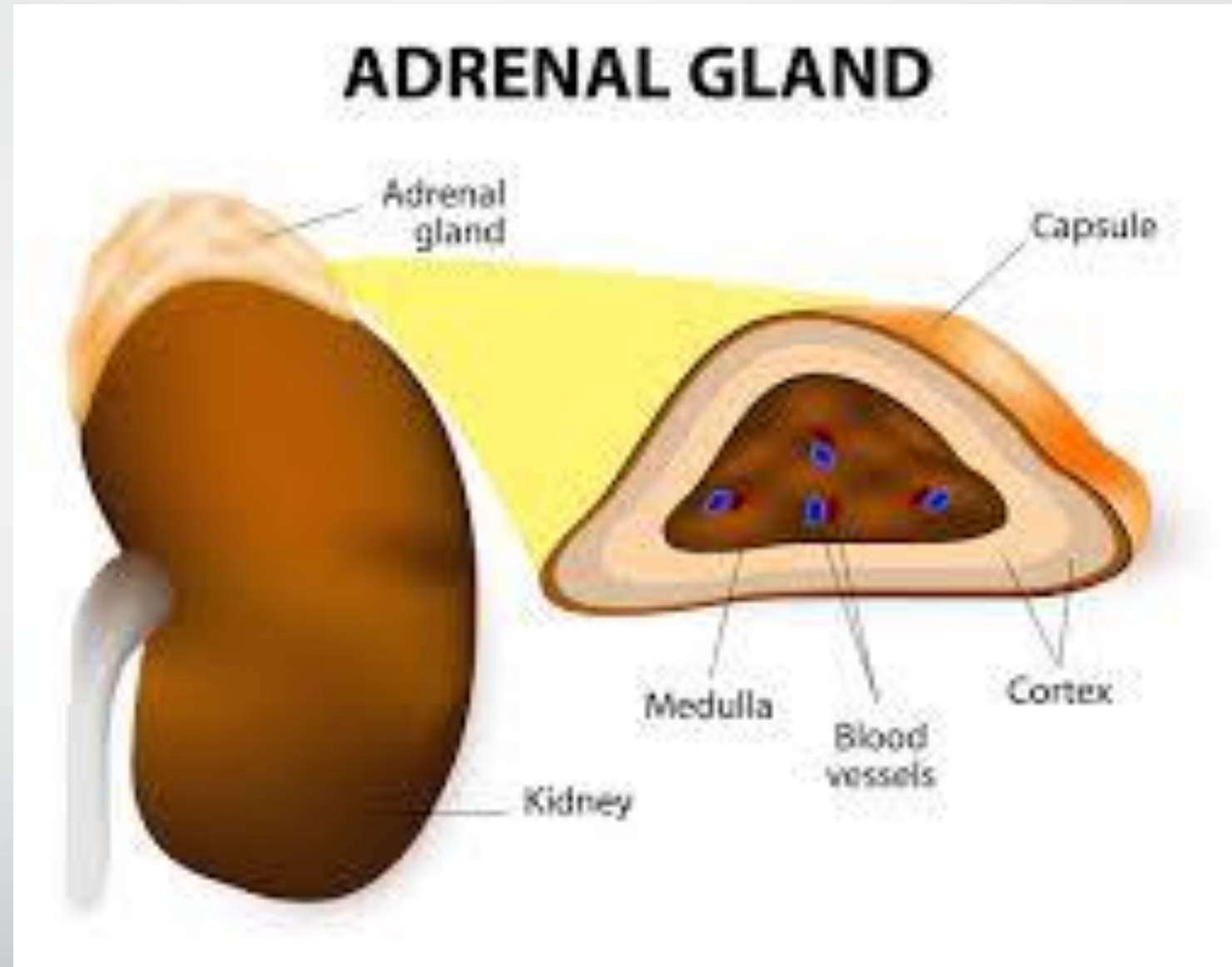
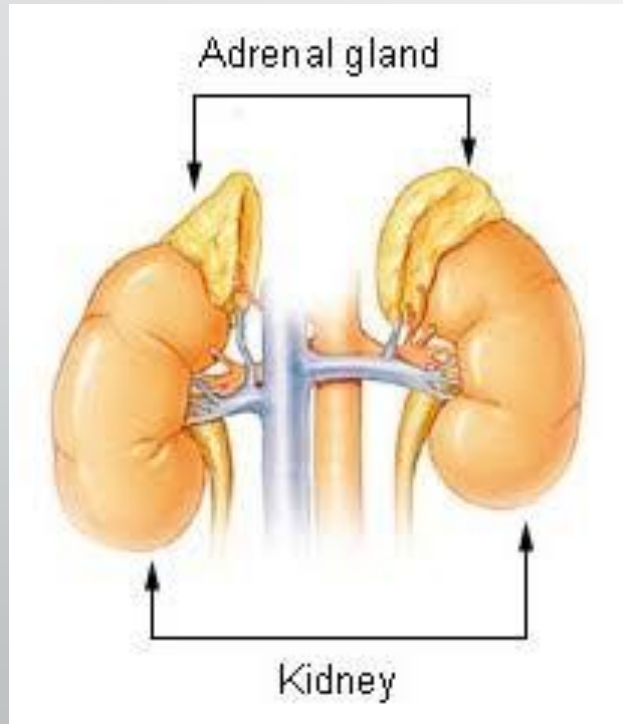
Allegheny School of Anesthesia



O B J E C T I V E S

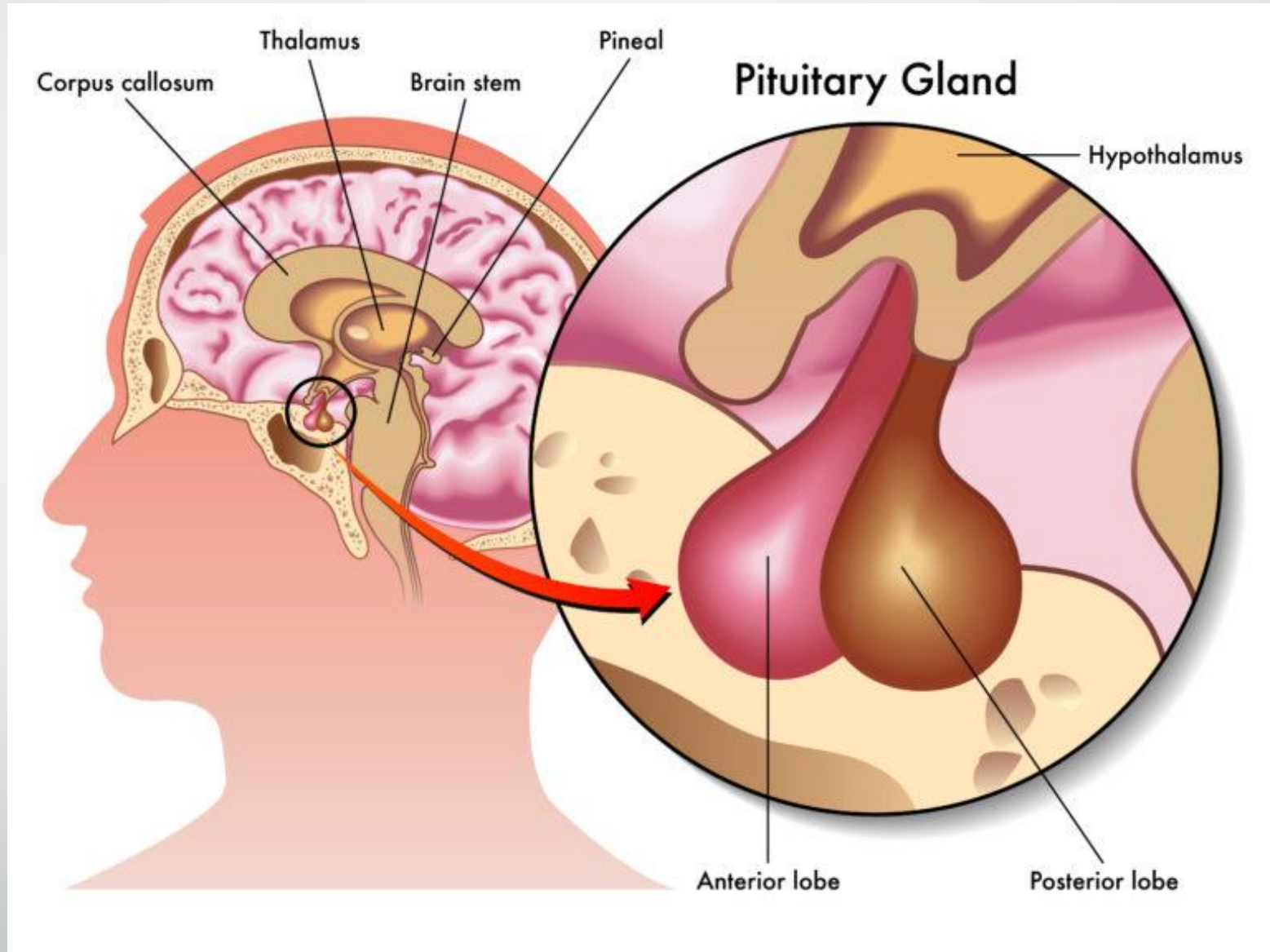
- Review A&P of adrenal gland & HPA axis
- Review circadian rhythm and cortisol cycle
- Discuss hyperadrenocorticism
- Discuss physiology of adrenal insufficiency and Addisonian Crisis
- Identify conditions/situations which can cause adrenal insufficiency, possibly requiring steroid dosing
- Discuss treatment options and goal-directed therapies
- Compare glucocorticoid and mineralocorticoid effects of glucocorticoids
- Review anesthesia considerations for patients with adrenal insufficiency
- Discuss literature review and case studies

Adrenal Gland Anatomy



Corticotropin Releasing Hormone

Hypothalamus secretes CRH
Target Site- Anterior Pituitary



Factors affecting CRH release

Fever

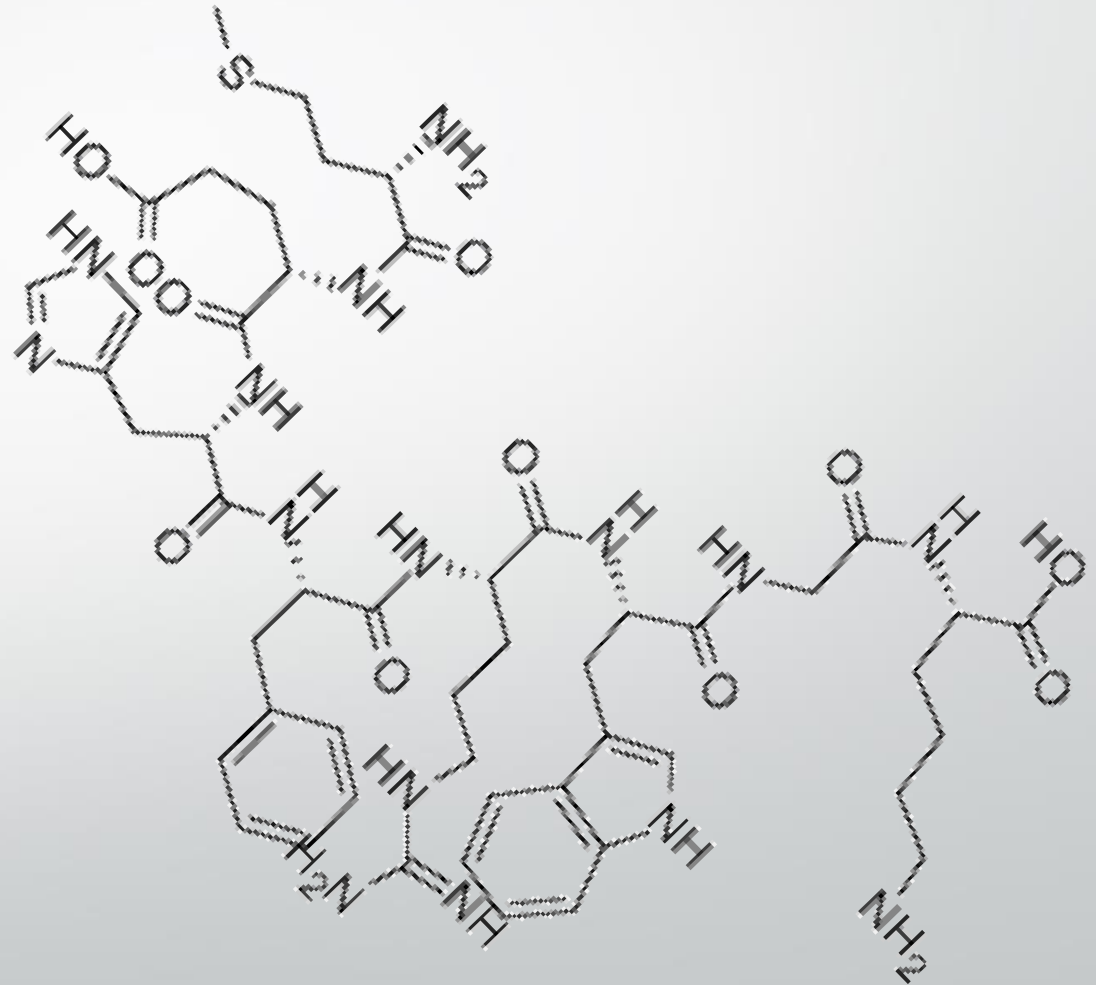
Stress

Hypoglycemia



ACTH

- The anterior pituitary is stimulated by the hypothalamic corticotropin-releasing hormone (CRH)
- (CRH) – daily rhythmic cycle
- The anterior pituitary secretes ACTH
- ACTH targets receptors on the adrenal cortex.



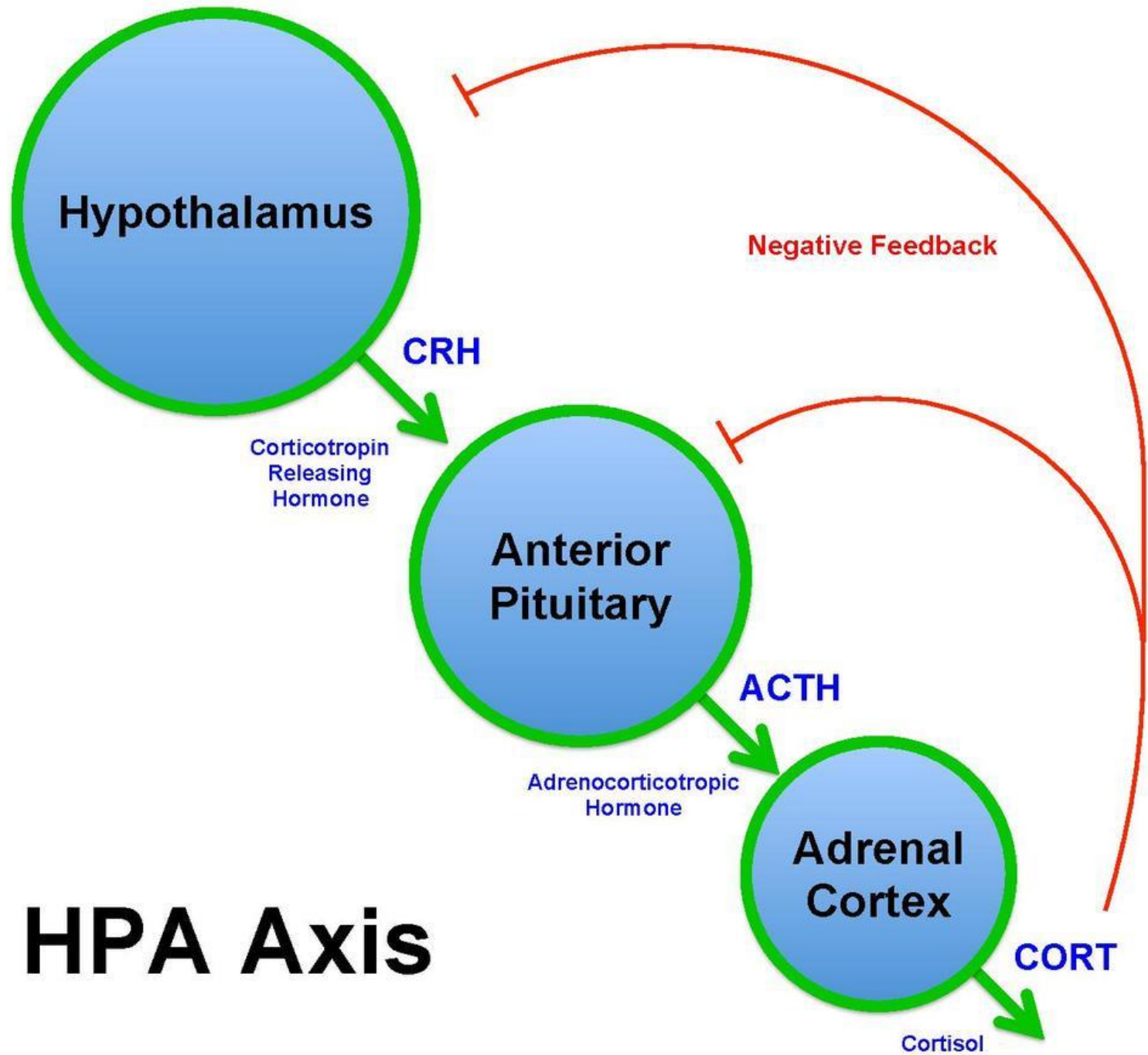
Adrenal Hormones

- **Adrenal Cortex:**

ACTH released by the anterior pituitary binds with receptor sites on the adrenal cortex to stimulate the release of mineralocorticoids and glucocorticoids

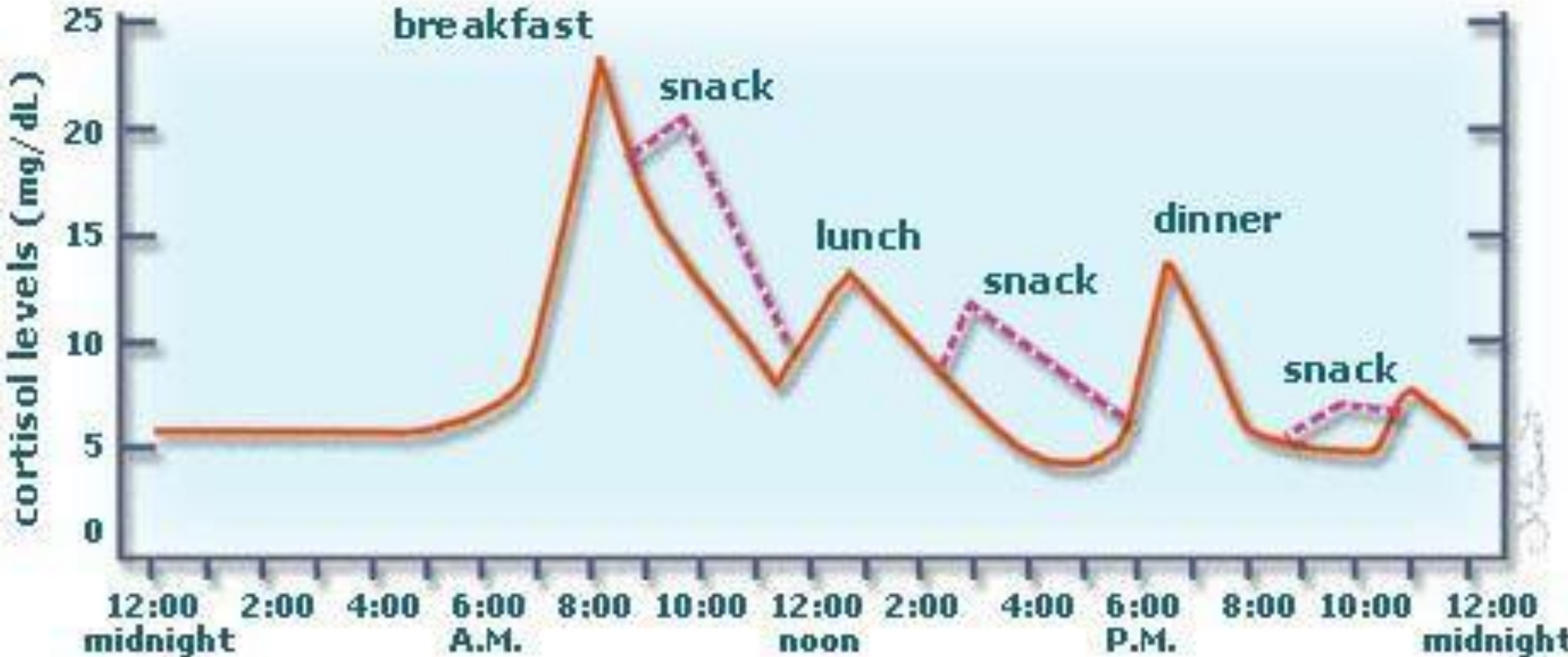
- **Adrenal Medulla:**

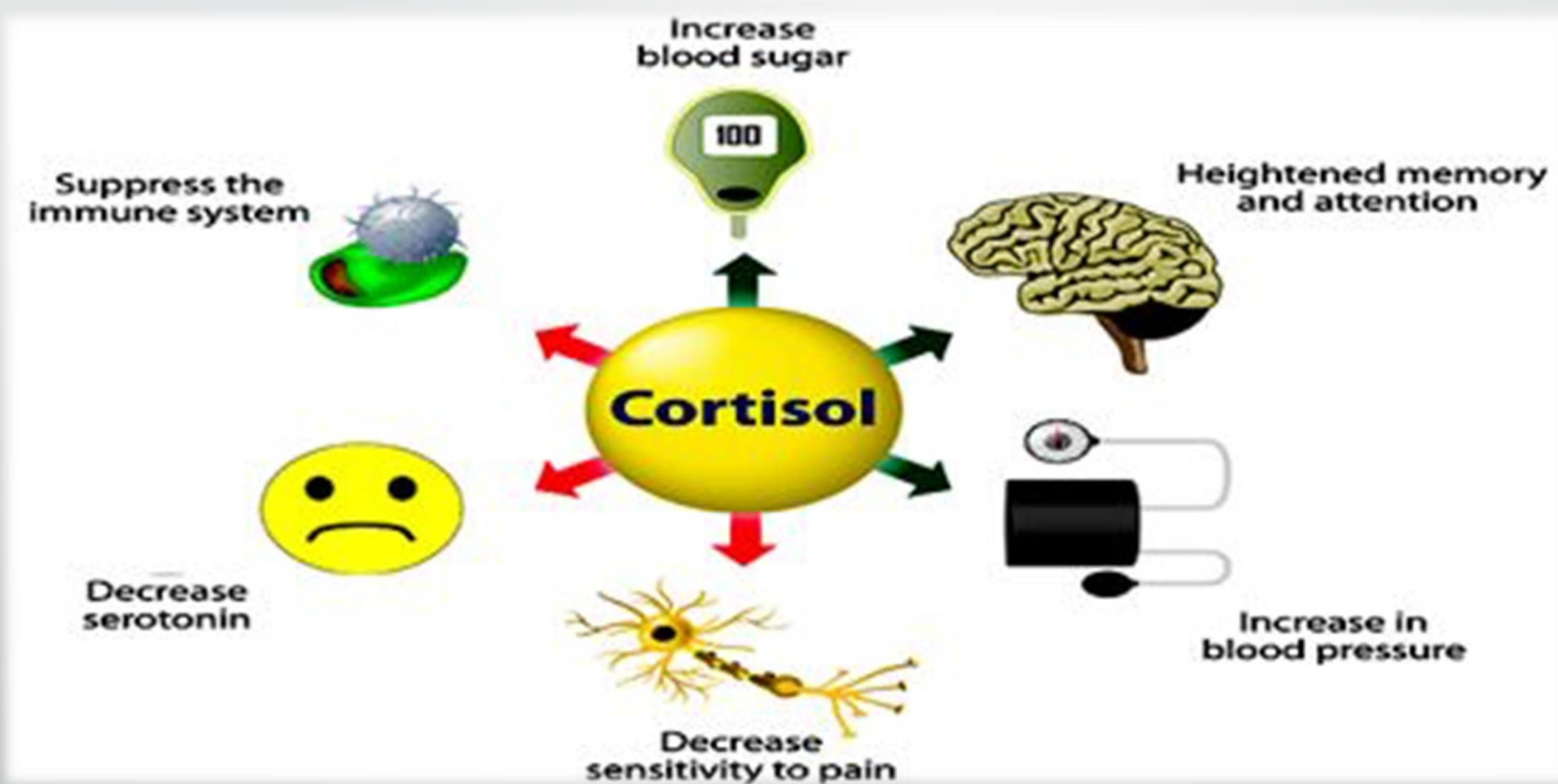
Preganglionic sympathetic nerve fibers stimulate the adrenal medulla to release epinephrine, norepinephrine, & dopamine



HPA Axis

Circadian rhythm and cortisol cycle





Adrenal Hyperfunction

- **Cushing's Syndrome - Classic Presentation**
 - **Moon face**
 - **Striations of the skin**
 - **HTN**
 - **Truncal obesity- thin extremities**
 - **Diffuse ecchymosis**
 - **Hypervolemia**

Adrenal Hypofunction

- **Adrenocortical Insufficiency**
 - **Primary**
 - **Secondary**
 - **Acute Adrenal Crisis**

Addison's Disease

- **First described in 1855**
- **Primary adrenocortical insufficiency becomes apparent when 90% of the gland is destroyed.**
- **TB is a common cause of Addison's Disease worldwide.**
- **Domestically – most commonly due to autoimmune dysfunction**
- **May also be associated with Type I Diabetes or Hashimoto's thyroiditis**
- **Less commonly related to congenital defect, sarcoidosis, HIV, adrenal hemorrhage, malignancy, or trauma**

Addisonian Crisis

Sudden onset of severe adrenal insufficiency

Rare → High morbidity and mortality if unrecognized

Adrenal insufficiency can progress rapidly with inadequate adrenal reserves:

- Stress**
- Surgery**
- Sepsis**
- Acute illness**

Perioperative adrenal crisis:

Medical emergency requiring rapid intervention

Signs & Symptoms

- **Weakness & fatigue*****
- **Weight loss & reduced appetite**
- **Abdominal pain**
- **Vomiting or diarrhea**
- **Often associated with hypoglycemia**
- **Hyperpigmentation**
- **Volume depletion: hyperkalemia, hyponatremia**

Treatment

- **Early identification: associated hypoglycemia, hypovolemia, electrolyte imbalances**
- **Rapid IV glucose containing isotonic crystalloid solution**
- **Advanced hemodynamic monitoring and inotropic support**
- **Steroid replacement**
 - **Rescue drug of choice: hydrocortisone 100mg**
 - **Followed by 100-200mg over 24^o**

Related Conditions

Primary Adrenal Suppression

Adrenal hemorrhage or infarction

Infectious:

Tuberculosis

Human immunodeficiency virus

Syphilis

Disseminated fungal infection

African trypanosomiasis

Continued...

- **Metastatic cancer**
- **Medications: azole antifungals, barbiturates, phenytoin, rifampin, megestrol acetate**
- **Other: congenital adrenal hypoplasia, familial glucocorticoid deficiency, impaired steroid biosynthesis, & impaired cholesterol biosynthesis**

HPA Axis Suppression & ACTH Deficiency 2° hypothalamic or pituitary gland dysfunction

Long-term treatments with exogenous glucocorticoid therapy → decreased ACTH output and eventually adrenal cortex atrophy; Comparative studies contain broad variability.

- Symptoms similar to primary adrenal insufficiency**
 - Less likely associated with hypovolemia or electrolyte abnormalities**

Complications of Exogenous Steroids

- Sodium retention and edema
- Hyperglycemia
- Susceptibility to infections
- Osteoporosis
- Cataracts
- Seizures
- Peptic ulcer disease
- Hypokalemia

Etomidate

- Short-acting hypnotic agent: commonly used in cardiac patients d/t relative cardiovascular stability
- Inhibits cortisol synthesis- dose dependent fashion
- Can suppress adrenal function for 4-8 °
- Cortisol levels also decrease post cardiac surgery- stimulus to release high levels of endogenous stress hormones
- Can progress to ARDS

Corticosteroid	Daily Secretion	Mineralocorticoid Effect	Glucocorticoid Effect	Anti-Inflammatory Effect
Aldosterone	0.125 mg	3,000 mg	0	insignificant
Desoxy-Corticosterone	--	100 mg	0	0
Cortisol	20 mg	1 mg	1 mg	1 mg
Cortisone & Corticosterone	Minimal	0.8 mg 15 mg	0.8 mg 0.35 mg	0.8 mg 0.3 mg



Comparative Pharmacology

<i>Steroid</i>	<i>Common Name</i>	<i>Glucocorticoid Effect</i>	<i>Mineralocorticoid Effect</i>	<i>Equivalent Dosage</i>	<i>Duration of Action (Hrs)</i>
Cortisol	Hydrocortisone Solu-Cortef	1	1	20	8-12
Cortisone	Cortone	0.8	0.8	25	8-36
Prednisolone	Prelone	4	0.8	5	12-36
Prednisone *	Deltasone	4	0.8	5	18-36
Methylprednisolone *	Medrol Solu-Medrol	5	0.5	4	12-36
Dexamethasone	Decadron	25	0	0.75	36-54
Fludrocortisone	Florinef	10	250	2	24

- **Herbal Remedy: adrenal suppression**

Published in 2014: Results of small patient study group performed by rheumatologist, pharmacologist, & chemists.

- Herbal medicine prevalence (CAM)
- Rapidly becoming popular in management of RA
- Failure to disclose
- Long-term use with adverse sequelae

CASE- #1 49y Male

- **Polyarthritic Disease: asymptomatic for 10 years.**
- **Developed fatigue, muscle weakness, and suicidal tendencies**
- **Evaluated by rheumatologist**
 - Prior to this he was taking herbal supplement (powder) for 3 years and then discontinued it.

Results:

- Serum cortisol: 0.32 ug/mL; WNL: (6.2-19.4 ug/mL)
- Vit D deficiency: 11.93 ng/mL; WNL: (30-70 ng/mL)
Insufficient (21-30) Deficient (< 20)
- Erythrocyte sed rate: 44mm/h; WNL: (3-10mm/h)
- Uric acid Level: 11.1; WNL: (2-7 mg/dL)
- Negative rheumatoid factor
- Initiated on methotrexate, colchicine, febuxostat, & *deflazacort*
- Presumed to be due to betamethasone or dexamethasone in herbal supplement

CASE- #2 38y old Male

- Polyarthritic disease: 5 years taking herbal supplement
- Developed morning stiffness, joint swelling and deformity
- Evaluated by rheumatologist
 - Positive rheumatoid factor: 48mg/dL; WNL: (<20)
 - Therapy: prednisolone, folic acid, famotidine, & methotrexate

- Herbal powders tested utilizing mass spectrometry
- Case 1: Powder showed correlation of a compound that could be either betamethasone or dexamethasone based on its mass spectrometry results.
- Case 2: Inconclusive data due to numerous compounds, confounding the testing results.

Caveat of Etomidate in Cardiac Patients

Research with ascorbic acid on prevention of adrenal cortical suppression r/t etomidate

Patients: Males & females, Ages 25-60, NYHA status < IV, elective cardiac surgery, utilizing Etomidate for induction.

Gp 1: Vit C 500mg BID for 7 days

Gp 2: Placebo BID for 7 days

Randomization based on computer selection

Double blinded to managing staff

Cortisol & lactate: Pre-op, 10' before induction, 3 min after laryngoscopy, after sternotomy, at 1h after cross clamp & clamp release, 6, 12, 24hour marks

Ascorbic Acid Trials

- 78 patients randomly selected in double blinded fashion - 6 refused & during operation 2 fell out of inclusion criteria based on CC > 2h
- 35 patients in each study group
- 1h post induction
 - Gp I: Cortisol 69.51 +/- 7.65 Gp II: 27.74 +/-4.72
- This trend continued in a linear fashion for 24h after induction.
- 24 h: Total requirement for adrenaline
 - Gr I: 2.83 +/- 1.27 Gr II: 3.40 +/- 1.09

Surgery Type	Endogenous Cortisol Secretion Rate	Examples	Recommended Steroid Dosing
Superficial	8–10 mg per day (baseline)	Dental surgery Biopsy	Usual daily dose
Minor	50 mg per day	Inguinal hernia repair Colonoscopy Uterine curettage Hand surgery	Usual daily dose <i>plus</i> Hydrocortisone 50 mg IV before incision Hydrocortisone 25 mg IV every 8 h × 24 h Then usual daily dose
Moderate	75–150 mg per day	Lower extremity revascularization Total joint replacement Cholecystectomy Colon resection Abdominal hysterectomy	Usual daily dose <i>plus</i> Hydrocortisone 50 mg IV before incision Hydrocortisone 25 mg IV every 8 h × 24 h Then usual daily dose
Major	75–150 mg per day	Esophagectomy Total proctocolectomy Major cardiac/vascular Hepaticojejunostomy Delivery Trauma	Usual daily dose <i>plus</i> Hydrocortisone 100 mg IV before incision Followed by continuous IV infusion of 200 mg of hydrocortisone more than 24 h <i>or</i> Hydrocortisone 50 mg IV every 8 h × 24 h Taper dose by half per day until usual daily dose reached <i>plus</i> Continuous IV fluids with 5% dextrose and 0.2–0.45% NaCl (based on degree of hypoglycemia)

Clinical Guidelines

Data from Axelrod,⁴ Salem *et al.*,¹³ and Bornstein *et al.*⁶

IV = intravenous.

Steroid Considerations

- Glucocorticoids penetrate the BBB & decrease edema associated with mass lesions.
- In the absence of mass lesions, glucocorticoids may produce a pseudotumor cerebri effect (\uparrow ICP) and papilledema.
- Complications: hyperglycemia, glucosuria, GI bleeding, electrolyte imbalances and \uparrow infection
- Recent data regarding steroids show they may be harmful when given for intracranial HTN resulting from TBI.
- Hours are necessary for ICP decompression to even become apparent.

Anesthesia Considerations

- *** Identify primary vs. secondary adrenal insufficiency risk factors**
- **Thoroughly assess patient to include all medicinal therapies.**
- **Select proper supplement, if required, based on preoperative evaluation and surgical requirements**
- **Avoid etomidate**



Relaxation

Stress

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